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WOODCOCK WASHBURN LLP
ONE LIBERTY PLACE 46TH FLR.
PHILADELPHIA, PA 19103

EXAMINER
TRAN, MY CHAU T

ART UNIT	PAPER NUMBER
1639	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/813,408	Applicant(s) DELAGRAVE ET AL.	
	Examiner My-Chau T. Tran	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 11-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment filed 6/26/03 in Paper No. 11 is acknowledged and entered. Claims 10, and 23-56 are canceled by the amendment. Claims 1 and 11 are amended by the amendment.

2. Claims 1-9 and 11-22 are pending.

Election/Restrictions

3. Applicants request rejoinder of claims 11-22 with claims 1-9 because applicants have amended claim 11 to depend from claim 1 have been considered. Claims 11-21 are now rejoined with claims 1-9. However, **claim 22** is not a method claim thus claim 22 is still withdrawn.

4. Claim 22 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8.

5. Claims 1-9 and 11-21 are treated on the merit in this Office Action.

Withdrawn Rejections

6. The previous objection for the disclosure because it contains an embedded hyperlink and/or other form of browser-executable code such as pg. 19 (line 30), pg. 20 (line 23), pg. 21 (line 4 and 21), pg. 35 (line 7) and others throughout the specification has been withdrawn in

view of applicant's amendments of the specification by deleting the embedded hyperlink and/or other form of browser-executable code.

7. The previous rejections 35 USC 112, second paragraph, for claims 1-9 have been withdrawn in view of applicant's amendments of claim 1and arguments.

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Maintained Rejections

Claim Rejections - 35 USC § 102

9. Claims 1-2, 4-6, and 8-9 are rejected under 35 U.S.C. 102(e) as being anticipated by Barany et al. (US Patent 6,506,594 B1).

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of ligating the oligonucleotides with ligase. The oligonucleotides are amplified prior to assembling the polynucleotide. The method further comprise of attaching the oligonucleotides to a solid support."

Barany et al. disclose a method for identifying one or more of a plurality of sequences in a plurality of target nucleotide sequences. The method comprise of a ligation phase, a capture phase, and a detection phase (Abstract; col. 5, lines 25-30). The ligation phase comprise of a plurality of oligonucleotides sets wherein each set includes a first oligonucleotide probe, having

a target-specific portion and an addressable array-specific portion, and a second oligonucleotide probe, having a target-specific portion and a detectable reporter label (col. 5, lines 33-41). The first and second oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence. Prior to the ligation detection reaction phase the sample is preferably amplified by PCR (col. 14, lines 13-15; col. 14, lines 38-67 to col. 15, lines 1-4). The method further comprise of forming an array of oligonucleotides on a solid support (col. 6, lines 18-29). Therefore, the method of Barany et al. anticipates the presently claimed invention.

Response to Arguments

10. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by Barany et al. (US Patent 6,506,594 B1) for claims 1-2, 4-6, and 8-9 were considered but they are not persuasive for the following reasons.

Applicant alleges that the method of Barany et al does not anticipate the presently claimed method because the coupled oligonucleotides of Barany et al. do not share a terminal region of sequence and that the amplification occurs prior to the ligation reaction. Therefore, the method of Barany et al does not anticipate the presently claimed method.

Applicant's arguments are not convincing since the method of Barany et al. does anticipate the presently claimed method. Barany et al. do disclose that the coupled oligonucleotides share a terminal region of sequence (col. 6, lines 18-29) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would

share a terminal region of sequence as disclose on col. 6, lines 18-29. Thus Barany et al. do disclose that the coupled oligonucleotides share a terminal region of sequence. Barany et al. also disclose "coupling" that refers to "[t]he covalent joining of oligonucleotides at their ends to form a linear coupled oligonucleotides" (col. 11, lines 14-18; col. 14, lines 13-15). Additionally, Barany et al. disclose that "the ligation phase can be preceded by an amplification process" (Abstract, lines 16-17) (e.g. the amplification occurs prior to the ligation reaction). Therefore, the method of Barany et al does anticipate the presently claimed method.

11. Claims 1-2, and 4-5 are rejected under 35 U.S.C. 102(e) as being anticipated by Harney (Us Patent 6,495,318 B2).

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of ligating the oligonucleotides with ligase. The method further comprise of attaching the oligonucleotides to a solid support."

Harney disclosed a method of solid phase synthesis wherein the nucleic acid components (oligonucleotides) can be linked sequentially to form the nucleic acid construct (polynucleotides) (col. 28, lines 4-26). The method comprise of attachment to a solid support as a starting point in the assembly of a series of nucleic acid components, in a defined order, to form a multicomponent nucleic acid construct. The initial nucleic acid component is attached to a solid support. Additional nucleic acid components, designed to contain unique terminal sequences at

either end, are added in a step-wise fashion, as single components or non-functional multicomponent constructs, and the assembly of components is based on the specific annealing of complementary terminal sequence pairs. Nucleic acid components may be ligated together, using a ligase enzyme, after each nucleic acid component addition step in the assembly of the larger construct. Therefore, the method of Harney anticipates the claimed invention.

Response to Arguments

12. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by Harney (Us Patent 6,495,318 B2) for claims 1-2, and 4-5were considered but they are not persuasive for the following reasons.

Applicant contends that the method of Harney does not anticipate the presently claimed method because the coupled oligonucleotides of Harney do not share a terminal region of sequence. Therefore, the method of Harney does not anticipate the presently claimed method.

Applicant's arguments are not convincing since the method of Harney does not anticipate the presently claimed method. The coupled oligonucleotides of Harney do share a terminal region of sequence (col. 28, lines 4-26) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 26, lines 4-26. Thus the method of Harney does anticipate the presently claimed method.

13. Claims 1, 4-5, 7-8, and 11-15 (*rejoined claims*) are rejected under 35 U.S.C. 102(e) as being anticipated by Huang et al. (US Patent 6,489,466 B2).

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of blocking one end of at least one of the oligonucleotides prior to coupling. The method further comprise of attaching the oligonucleotides to a solid support."

Huang et al. disclosed a method of immobilizing oligonucleotide to a substrate (solid support) (col. 1, lines 37-40). The method comprises of a method for an oligonucleotide synthesis (col. 2, lines 17-35). The method covers a deprotection-activation-coupling oligonucleotide synthesis which consists of a nucleotide or an oligonucleotide having a free terminal C-3' hydroxyl and a terminal C-5' that is blocked by a group, wherein the free terminal C-3' hydroxyl is activated with a phosphorous activating group. Therefore, the method of Huang et al. anticipates the presently claimed invention.

With regard to claim 15, the solid support comprise of materials such as glass (col. 6, lines 23-32). The oligonucleotides comprise bases of the range of 10 to 1000 (col. 16, lines 1-7) (refers to claim 13).

Response to Arguments

14. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by Huang et al. (US Patent 6,489,466 B2) for claims 1, 4-5, and 7-8 were considered but they are not persuasive for the following reasons.

Applicant argues that the method of Huang et al. does not anticipate the presently claimed method because the coupled oligonucleotides of Huang et al. do not share a terminal region of sequence. Therefore, the method of Huang et al. does not anticipate the presently claimed method.

Applicant's arguments are not convincing since the method of Huang et al. does not anticipate the presently claimed method. The coupled oligonucleotides of Huang et al. do share a terminal region of sequence (col. 2, lines 17-35) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 2, lines 17-35. Thus the method of Huang et al. does anticipate the presently claimed method.

15. Claims 1-5, 7-9, and 11-19 (*rejoined claims*) are rejected under 35 U.S.C. 102(e) as being anticipated by Delagrave (US Patent 6,479,262 B1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of ligating the oligonucleotides with ligase and wherein at least one of the oligonucleotide of the coupled oligonucleotide is blocked at one end prior to the coupling. The ligase is T4 RNA ligase. The method further comprise of attaching the oligonucleotides to a solid support."

Delagrave disclosed a method of preparing polynucleotides on a solid support wherein the polynucleotides are assembled in either direction (e.g. 5'to 3' or 3' to 5') by ligating a plurality of oligonucleotides (Abstract; col. 3, lines 8-35). The method comprise of contacting the solid support with an oligonucleotide from a plurality of oligonucleotides to form a tethered oligonucleotide (col. 5, lines 38-46; col. 8, lines 15-21). The tethered oligonucleotide is ligated with T4 RNA ligase to another oligonucleotide thereby assembling the polynucleotide (col. 6, lines 30-49). To avoid excessive accumulation of failed sequences, a capping step is performed (col. 7, lines 26-42; col. 8, lines 61-66). Therefore, the method of Delagrave anticipates the presently claimed invention.

Delagrave further disclose that the solid support comprises polymer such as polystyrene, and polyacrylamide (col. 5, lines 26-34) (refers to claim 15). The length of the polynucleotides comprises at least 200 nucleotides (col. 4, lines 31-65).

Response to Arguments

16. Applicant's argument(s) directed to the above rejection under 35 USC 102(e) as being anticipated by Delagrave (US Patent 6,479,262 B1) for claims 1-5, and 7-9 were considered but they are not persuasive for the following reasons.

Applicant alleges that the method of Delagrave does not anticipate the presently claimed method because the coupled oligonucleotides of Delagrave do not share a terminal region of sequence. Therefore, the method of Delagrave does not anticipate the presently claimed method.

Applicant's arguments are not convincing since the method of Delagrave does anticipate the presently claimed method. Delagrave do disclose that the coupled oligonucleotides share a terminal region of sequence (col. 5, lines 38-46; col. 8, lines 15-21) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 5, lines 38-46 and col. 8, lines 15-21. Thus Delagrave do disclose that the coupled oligonucleotides share a terminal region of sequence. Delagrave also disclose "coupling" that refers to "[t]he covalent joining of oligonucleotides at their ends to form a linear coupled oligonucleotides" (col. 6, lines 30-49). Therefore, the method of Delagrave anticipates the presently claimed method.

Claim Rejections - 35 USC § 103

17. Claims 1-6, and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. (US Patent 6,506,594 B1) in view of Walker et al. (*PNAS*, **1975**, 72(1):122-126).

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of ligating the oligonucleotides with ligase wherein the ligase is T4 RNA ligase. The oligonucleotides are amplified prior to assembling the polynucleotide. The method further comprise of attaching the oligonucleotides to a solid support."

Barany et al. disclose a method for identifying one or more of a plurality of sequences in a plurality of target nucleotide sequences. The method comprise of a ligation phase, a capture phase, and a detection phase (Abstract; col. 5, lines 25-30). The ligation phase comprise of a plurality of oligonucleotides sets wherein each set includes a first oligonucleotide probe, having a target-specific portion and an addressable array-specific portion, and a second oligonucleotide probe, having a target-specific portion and a detectable reporter label (col. 5, lines 33-41). The first and second oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence. Prior to the ligation detection reaction phase the sample is preferably amplified by PCR (col. 14, lines 13-15; col. 14, lines 38-67 to col. 15, lines 1-4). The method further comprise of forming an array of oligonucleotides on a solid support (col. 6, lines 18-29).

The method of Barany et al. does not expressly disclose that the ligase is T4 RNA ligase.

Walker et al. disclosed a method of joining single-stranded oligonucleotides using T4 RNA ligase (Abstract). The RNA ligase has the advantage of not requiring the complementary strand, thereby simplifying the synthetic task (pg. 126, right col., lines 1-2).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the T4 RNA ligase as taught by Walker et al. in the method of Barany et al. One of ordinary skill in the art would have been motivated to include the T4 RNA ligase in the method of Barany et al. for the advantage of not requiring the complementary strand, thereby simplifying the synthetic task (Walker: pg. 126, right col., lines 1-2). Since both Barany et al. and Walker et al. disclose a method of coupling oligonucleotides by the method of ligation (Barany: col. 5, lines 33-41; Walker: Abstract).

Response to Arguments

18. Applicant's argument(s) directed to the above rejection under 35 USC 103(a) as being unpatentable over Barany et al. (US Patent 6,506,594 B1) in view of Walker et al. (*PNAS*, **1975**, 72(1):122-126) for claims 1-6, and 8-9 were considered but they are not persuasive for the following reasons.

Applicant argues that the combination of Barany et al. (US Patent 6,506,594 B1) and Walker et al. (*PNAS*, **1975**, 72(1):122-126) is nonobvious over the presently claimed method because the coupled oligonucleotides of Barany et al. do not share a terminal region of sequence and that the amplification occurs prior to the ligation reaction. Therefore, the combination of Barany et al. and Walker et al. is nonobvious over the presently claimed method.

Applicant's arguments are not convincing since the combination of Barany et al. and Walker et al. is obvious over the presently claimed method. Barany et al. do disclose that the coupled oligonucleotides share a terminal region of sequence (col. 6, lines 18-29) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the

"coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 6, lines 18-29. Thus Barany et al. do disclose that the coupled oligonucleotides share a terminal region of sequence. Barany et al. also disclose "coupling" that refers to "[t]he covalent joining of oligonucleotides at their ends to form a linear coupled oligonucleotides" (col. 11, lines 14-18; col. 14, lines 13-15). Additionally, Barany et al. disclose that "the ligation phase can be preceded by an amplification process" (Abstract, lines 16-17) (e.g. the amplification occurs prior to the ligation reaction). Therefore, the combination of Barany et al. (US Patent 6,506,594 B1) and Walker et al. (*PNAS*, **1975**, 72(1):122-126) is obvious over the presently claimed method.

19. Claims 1, and 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huang et al. (US Patent 6,489,466 B2) in view of Harney (Us Patent 6,495,318 B2).

"The presently claimed invention recites a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides. The coupling method step comprise of blocking one end of at least one of the oligonucleotides prior to coupling. The oligonucleotides are amplified prior to assembling the polynucleotide. The method further comprise of attaching the oligonucleotides to a solid support."

Huang et al. disclosed a method of immobilizing oligonucleotide to a substrate (solid support) (col. 1, lines 37-40). The method comprise of deprotection-activation-coupling oligonucleotide synthesis wherein one end to the oligonucleotide is block (col. 2, lines 17-35).

The method of Huang et al. does not expressly disclose that a method step of amplification of the coupled oligonucleotide.

Harney disclosed a method of solid phase synthesis wherein the nucleic acid components (oligonucleotides) can be linked sequentially to form the nucleic acid construct (polynucleotides) (col. 28, lines 4-26). The method comprise of attachment to a solid support as a starting point in the assembly of a series of nucleic acid components, in a defined order, to form a multicomponent nucleic acid construct. The initial nucleic acid component is attached to a solid support. Additional nucleic acid components, designed to contain unique terminal sequences at either end, are added in a step-wise fashion, as single components or non-functional multicomponent constructs, and the assembly of components is based on the specific annealing of complementary terminal sequence pairs. Nucleic acid components may be ligated together, using a ligase enzyme, after each nucleic acid component addition step in the assembly of the larger construct. The method further comprise of the method of PCR amplification (col. 13, lines 51-61). The method provides a rapid construction of customized constructs without the need to use restriction enzymes (col. 4, lines 5-8).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include a method step of amplification of the coupled oligonucleotide as taught by Harney in the method of Huang et al. One of ordinary skill in the art would have been motivated to include a method step of amplification of the coupled oligonucleotide in the method of Huang et al. for the advantage of providing a rapid construction of customized constructs without the need to use restriction enzymes (Harney: col. 4, lines 5-8). Since both Huang et al. and Harney disclose a method of immobilizing oligonucleotides to a substrate wherein the

oligonucleotides are constructs of nucleic acid components (Huang: col. 1, lines 37-40; Harney: col. 28, lines 4-11).

Response to Arguments

20. Applicant's argument(s) directed to the above rejection under 35 USC 103(a) as being unpatentable over Huang et al. (US Patent 6,489,466 B2) in view of Harney (Us Patent 6,495,318 B2) for claims 1, and 4-9 were considered but they are not persuasive for the following reasons.

Applicant contends that the combination of Huang et al. (US Patent 6,489,466 B2) and Harney (Us Patent 6,495,318 B2) is nonobvious over the presently claimed method because the coupled oligonucleotides of both Huang et al. and Harney do not share a terminal region of sequence. Therefore, the combination of Huang et al. and Harney is nonobvious over the presently claimed method

Applicant's arguments are not convincing since the combination of Huang et al. and Harney is obvious over the presently claimed method. The coupled oligonucleotides of Huang et al. do share a terminal region of sequence (col. 2, lines 17-35) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 2, lines 17-35. The coupled oligonucleotides of Harney do share a terminal region of sequence (col. 28, lines 4-26) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the

"coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose on col. 26, lines 4-26. Thus the combination of Huang et al. and Harney is obvious over the presently claimed method.

Double Patenting

21. Claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the presently claimed invention, which is a method of preparing a polynucleotide having a target sequence from a plurality of oligonucleotides. The method comprise of coupling the oligonucleotides to form a plurality of coupled oligonucleotides, and assembling the polynucleotide by extension of the coupled oligonucleotides, would encompass that of the claimed invention of US Patent 6,479,262 B1, which is a method of preparing a polynucleotide having at least 200 nucleotides and a predetermined nucleotide sequence. The method step comprises contacting said solid support with the 3′ terminus of a fist oligonucleotide from said plurality of oligonucleotides to form a tethered oligonucleotide, ligating the 3′ terminus of another oligonucleotide from said plurality of oligonucleotides to the 5′ terminus of the tethered oligonucleotide, phosphorylating the 5′ terminus of said another oligonucleotide, and repeating the steps of ligation and phosphorylation until said polynucleotide is prepared.

Response to Arguments

22. Applicant's argument(s) directed to the above rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 10, 12, 14, 18, and 24-26 of U.S. Patent No. 6,479,262 B1 were considered but they are not persuasive for the following reasons.

Applicant argues that the obviousness-type double patenting rejection of claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1 (Delagrave) is improper because the patent claims of Delagrave does not teach that the coupled oligonucleotides share a terminal region of sequence. Thus the present claims are "[m]ore than mere obvious variations over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of Delagrave.

Applicant's arguments are not convincing since the obviousness-type double patenting rejection of claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) as being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1 (Delagrave) is proper. The claims of Delagrave do disclose that the coupled oligonucleotides share a terminal region of sequence (claims 10 and 20) for the term "coupling" as indicated by applicant "[i]s defined in the specification on page 10, lines 4-6, as the covalent joining of two molecules" (see response pg. 11, lines 2-3) would encompass the "coupling" of an array of oligonucleotides to the solid support in which case the array of oligonucleotides would share a terminal region of sequence as disclose in claims 10 and 20. Thus the obviousness-type double patenting rejection of claims 1-5, 7-8, 11-15 (*rejoined claims*), and 17-18 (*rejoined claims*) as

being unpatentable over claims 1, 7, 10, 12, 14, 18, 20-21, and 24-26 of U.S. Patent No. 6,479,262 B1 (Delagrave) is proper.

New Rejections – Necessitated by Amendment

Claim Rejections - 35 USC § 112

23. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

24. Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, the acronym ddUTP is not defined in the claim so that those who are ordinary skills in the art would know applicant intended meaning. It should be define on its first appearance.

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 1 and 11-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delagrave (US Patent 6,479,262 B1) and Barany et al. (US Patent 6,506,594 B1).

Delagrave disclosed a method of preparing polynucleotides on a solid support wherein the polynucleotides are assembled in either direction (e.g. 5'to 3' or 3' to 5') by ligating a plurality of oligonucleotides (Abstract; col. 3, lines 8-35). The method comprise of contacting the solid support with an oligonucleotide from a plurality of oligonucleotides to form a tethered oligonucleotide (col. 5, lines 38-46; col. 8, lines 15-21). The tethered oligonucleotide is ligated with T4 RNA ligase to another oligonucleotide thereby assembling the polynucleotide (col. 6, lines 30-49). To avoid excessive accumulation of failed sequences, a capping step is performed (col. 7, lines 26-42; col. 8, lines 61-66). Delagrave further disclose that the solid support comprises polymer such as polystyrene, and polyacrylamide (col. 5, lines 26-34) (refers to claim 15). The length of the polynucleotides comprises at least 200 nucleotides (col. 4, lines 31-65).

The method of Delagrave does not expressly disclose that the method step of amplification the coupled oligonucleotides.

Barany et al. disclose a method for identifying one or more of a plurality of sequences in a plurality of target nucleotide sequences. The method comprise of a ligation phase, a capture phase, and a detection phase (Abstract; col. 5, lines 25-30). The ligation phase comprise of a

plurality of oligonucleotides sets wherein each set includes a first oligonucleotide probe, having a target-specific portion and an addressable array-specific portion, and a second oligonucleotide probe, having a target-specific portion and a detectable reporter label (col. 5, lines 33-41). The first and second oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence. Prior to the ligation detection reaction phase the sample is preferably amplified by PCR (col. 14, lines 13-15; col. 14, lines 38-67 to col. 15, lines 1-4). The method further comprise of forming an array of oligonucleotides on a solid support (col. 6, lines 18-29).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method step of amplification the coupled oligonucleotides as taught by Barany et al. in the method of Delagrave. One of ordinary skill in the art would have been motivated to include the method step of amplification the coupled oligonucleotides in the method of Barany et al. for the advantage of providing multiple copies of the same polynucleotides since both Delagrave and Barany et al. disclose the method of attaching the oligonucleotides to a solid support (Delagrave: col. 5, lines 38-46; col. 8, lines 15-21; Barany: col. 6, lines 18-29).

Conclusion

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner is on Increased Flex Schedule and can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

mct
September 21, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER